

REMARKS

Claims 1, 4-18, 20, 22, 24, and 27-31 were pending. Claims 1 and 20 are amended herein. Support for the amendments are found throughout the specification at, *inter alia*, ¶22 and ¶40, and thus it is believed that no new matter has been added. Claims 1, 4-18, 20, 22, 24, and 27-31 are pending. Claims 17 and 28 are allowed.

Applicants gratefully acknowledge the entry of the request for continued examination and the entry of the Amendment filed on April 22, 2004.

Applicants acknowledge with appreciation the allowance of claims 17 and 28.

Objections to the claims

Claims 1 and 20 are objected to because the amendment markings are confusing. Correction was requested.

Rejection Under 35 U.S.C. § 103 (a)

Claims 1, 4, 6-7, 10-12, 14-15, 18, 20, 22, and 29-30 are rejected under 35 U.S.C. § 103 (a) as allegedly being unpatentable over Jakobovits et al. in view of Edelman et al. (*Method. Enzymol.*) and Edelman et al. (U.S. Patent No. 3,843,324) for reasons of record. Claim 8, 16, 24, and 27 are rejected under 35 U.S.C. § 103 (a) as allegedly being unpatentable over Jakobovits et al. in view of Edelman et al (both references) as applied to claims 1, 20, and 22 above, and further in view of Chang (WO 84/03151) for reasons of record. Claims 5, 9, 27, and 31 are rejected as unpatentable under 35 U.S.C. § 103 (a) as allegedly being unpatentable over Jakobovits et al. in view of Edelman et al (both references) as applied to claim 1, and further in view of Kupchik for reasons of record. Claim 13 is rejected under 35 U.S.C. § 103 (a) as allegedly being unpatentable over Jakobovits et al. in view of Edelman et al (both references) as applied to claims 1, and further in view of Seifert (U.S. Patent 5,721,120) for reasons of record. Briefly, the Examiner alleges that lectins are not excluded as ligands useful in the claimed methods. The Examiner also asserts that there is no patentable weight in the inserted recitation of "wherein the microenvironment includes additional non-covalently associated cellular components." According to the Examiner, the

microenvironment of the receptor is so broad so as to include nothing associated with the receptor. Again, the Examiner dismisses the differences between the teachings of Jakobovits and Edelman. Applicant traverses these rejections.

Applicant respectfully submits that the cited combination of references fails to render the claimed methods *prima facie* obvious for reasons of record. The remarks below supplement those already provided.

The claims properly exclude lectin as a ligand, and therefore the cited combination of Jakobovits and Edelman (both references) fail to render the claimed methods obvious. Applicant notes that the specification clearly states that the ligand of the claimed methods do not encompass the use of lectin. *See, e.g.*, the specification at ¶22. An applicant is permitted to define terms using the specification as long as the language is sufficiently clear to inform the public of the metes and bounds of the claimed invention. *See* MPEP § 2173. In the instant application, Applicant properly excluded lectins from the definition of ligand in the specification *and thus the claims at issue*. Nonetheless, in an effort to expedite the prosecution, the claims are amended herein to incorporate the definition of ligand provided at ¶22 of the specification.

Applicant respectfully submits that “*all* words in a claim must be considered in judging the patentability of that claim against the prior art.” *See* MPEP § 2143.03 (citations omitted) (emphasis added). The limitation regarding the isolation of the microenvironment cannot properly be ignored. Contrary to the assertion of the Examiner, the limitation does not encompass a microenvironment that consists of nothing other than the receptor itself. By the plain language of the claim, the microenvironment “includes additional non-covalently associated cellular components.” Therefore, this limitation must be considered as it is written in the claim.

None of the references alone or in combination teach or suggest the use of non-lectin ligands to isolate a receptor and its associated microenvironment for analysis. The statement in Jakobovits at page 1489 is nothing more than a statement of current experiments. It contains no indication of whether the experiments worked or failed. Moreover, these experiments employ lectins, a ligand that is not employed in the instant methods and is fundamentally distinct from the receptors of the claimed methods for reasons previously discussed. For at least these reasons, the cited combination does not render the claimed methods obvious.

The cited combination of Jakobovits and Edelman also fail to teach the analysis of the receptor-associated microenvironment using the specific methods of chromatographic analysis of mass spectrometry. While the Examiner appears to dismiss this step of the claimed method because it has great breadth, Applicant respectfully submits that *all* claims limitations must be considered in an obviousness analysis. The cited references fail to teach this aspect of the claimed invention, thus failing to render the claims *prima facie* obvious.

Jakobovits, Edelman, and Chang

Applicant respectfully submits that the cited combination is not properly combinable because Chang's invention relies on cells retaining association with their membrane-bound receptors. As acknowledged by the Examiner, Chang teaches a test device having multiple antibody coated spots, each with an antibody directed against a different cell surface antigen. According to the Examiner, the antigen profiling taught by Chang renders the claimed method obvious. However, to combine these references is to simply combine apples and oranges. Chang discloses an antibody-based immunoassay used to detect antigen expression on the cell surface that requires that cells bind tightly to the antibody coated spots to permit detection in the assays. *See, e.g.*, Chang at page 6, lines 5-11. If Chang were modified according to the teaching of Jakobovits, the disclosed assay would not work. *See* MPEP § 2143.01 ("If the proposed modification or combination of the prior art would change the principle of operation of the prior art invention being modified, then the teaching of the references are not sufficient to render the claims *prima facie* obvious."). Therefore, for at least these reasons, this combination of references fails to render claims 8, 16, 24, and 27 *prima facie* obvious.

Jakobovits, Edelman, and Kupchik

The cited combination of Jakobovits and Edelman in view of Kupchik fails to render claims 5, 9, 27, and 31 *prima facie* obvious because Kupchik fails to teach the isolation of tumor antigens from whole cells. Kupchik teaches the production of monoclonal antibodies that are specific for carcinoembryonic antigen (CEA) and alphafetoprotein (AFP). Both CEA and AFP are circulating proteins whose increased levels in the serum indicate certain disease states, *e.g.*, malignancies. While CEA can also be membrane bound, Kupchik contains no discussion regarding antigen expression on cells in single cell suspension as in the claimed methods. For example,

Kupchik describes elevated CEA and AFP levels in the serum as useful diagnostic indicators. *See* Kupchik at page 82, first full paragraph and at 83, third full paragraph. The immunoadsorption discussed by Kupchik appears related only to handling these cell-free antigens without any disclosure regarding the isolation of antigens from cellular membranes. The mere fact that tumor antigens bound by antibodies is discussed is not enough to suggest to one of skill in the art to practice the method of claim 9. *See* MPEP § 2143.01 (“The mere fact that the references can be combined or modified does not render the resultant combination obvious unless the prior art also suggests the desirability of the combination.”) (citations omitted). Jakobovits fails to teach the use of antibodies, tumor cells, or any suggestion of isolating such antigens and their related microenvironment from tumor cells. Likewise, Edelman is completely silent. Thus, this combination of references fails to render the claimed methods *prima facie* obvious.

Jakobovits, Edelman, and Seifert

Applicant respectfully submits that Seifert adds nothing to the teachings of Jakobovits and Edelman. Seifert discloses a method of disrupting cells without harming the liberated cell products. *See* Seifert at Abstract. Seifert is completely silent regarding the isolation of a membrane-bound receptor that binds a particular ligand and is isolated with its microenvironment. In other words, Seifert teaches the complete disruption of a cell, recovery of the cellular contents, but nothing more. Thus, it fails to cure the deficiencies discussed above, or teach or suggest the use of sonication to successfully isolate a membrane-bound receptor and its microenvironment using a solid support coupled to a ligand that bind the receptor. In view of the failure to teach each and every element of the claims invention of claim 13, this combination of references fails to render the claimed method *prima facie* obvious.

Accordingly, the basis for this rejection may be removed.

Rejection Under the Judicially Created Doctrine of Obviousness-Type Double Patenting

Claims 1, 4-18, 20, 22, 24, and 27-31 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-4, 16-25, and 28-31 of co-pending Application Serial No. 10/209,328. According to the Examiner, the

conflicting claims are not identical, but they are not patentably distinct from each other because both sets of claims encompass common subject matter. Applicant traverses this rejection.

As no allowable subject matter has been indicated in either application, Applicant continues to request that this rejection be held in abeyance until such time. Applicant will submit a terminal disclaimer once allowable subject matter is indicated in the present application if it is required.

Applicant believes that the claim amendments and remarks made herein fully address all issues raised in the Office Action. Silence with regard to any of the Examiner's rejections is not an acquiescence to such rejections.

CONCLUSION

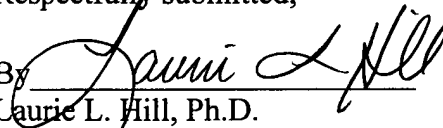
In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding objections and rejections of the claims and to pass this application to issue. If it is determined that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number given below.

In the event the U.S. Patent and Trademark office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket no. 511582006000. However, the Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

Dated: March 18, 2005

Respectfully submitted,

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